Primary Intraocular Posttransplantation Lymphoproliferative Disorder

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We report a case of posttransplantation lymphoproliferative disorder manifesting as an isolated, unilateral iris tumor. A 2-year-old boy who had undergone liver transplantation for biliary atresia at age 4 months was seen with a 2-month history of an enlarging iris nodule. Histopathologic examination of the iris lesion demonstrated a mixed population of lymphoid cells. To our knowledge, this is the youngest patient with posttransplantation lymphoproliferative disorder isolated to the eye.

Posttransplantation lymphoproliferative disorder (PTLD) develops in approximately 3% of patients who receive systemic immunosuppressive agents for liver transplantation. The spectrum of disease is broad and may range from aggregates of polyclonal lymphocytes to malignant, multisystem infiltration mimicking non-Hodgkin’s lymphoma. Although extranodal disease most commonly occurs in the gastrointestinal tract and central nervous system, lymphadenopathy and tumor infiltration of other tissues have been reported. Only 3 cases of intraocular PTLD have been described. We report in a child a case of PTLD that manifested as an isolated iris tumor with no evidence of associated ocular or systemic manifestations.

REPORT OF A CASE

A 2-year-old boy had a 2-month history of an enlarging iris mass. He had undergone liver transplantation at age 4 months for congenital biliary atresia. Because multiple biopsy specimens obtained in the postoperative period demonstrated no evidence of organ rejection or Epstein-Barr virus (EBV) infection, the patient was treated with low-dose cyclosporine (100 mg/d) and prednisone (0.45 mg/d). In the 4 months prior to presentation, he had received several courses of systemic antibiotics for upper respiratory tract infections, otitis media, and tonsillitis.

On examination, Teller visual acuity measured 13.0 cycles per centimeter in each eye. Ocular motility and primary gaze alignment were normal. Pupils were round and briskly reactive to light without afferent pupillary defect. Slitlamp examination of the right eye revealed a clear cornea with multiple granulomatous keratic precipitates inferiorly. The anterior chamber had cells (1+) and flare (2+). Examination of the iris showed a tan, cystic, diffuse, lobular thickening of the stroma inferiorly and inferotemporally, with prominent overlying blood vessels (Figure 1). Dilated fundus examination demonstrated no vitreous inflammation or retinal or choroidal lesions. Examination results from the left eye were completely normal (Figure 2). Echography demonstrated mild irregular thickening of the iris stroma with no evidence of posterior extension into the ciliary body (Figure 3).

Fine-needle aspiration biopsy specimens obtained from the superficial portion of the tumor demonstrated small lymphoid cells with occasional nuclear membrane abnormalities, plasma cells, and a few histiocytes, consistent with chronic inflammation or a lymphoid tumor. Inci-
sional biopsy consisting of a 4-clock-hour wedge resection of the lesion was subsequently performed with minimal hemorrhage.

Histopathologic examination revealed a dense infiltrate of small lymphoid cells with nuclear membrane abnormalities and occasional multiple and prominent nucleoli and rare mitotic figures (Figure 4). Occasional larger cells with large oval and irregularly shaped nuclei, prominent nucleoli, and moderately abundant cytoplasm were also present. No microorganisms were seen with special stains. Immunohistochemical stains demonstrated a polymorphic population of lymphocytes, including T cells (CD3) and B cells (CD20), with \( \lambda \) and \( \kappa \) light chains.

Systemic evaluation revealed no evidence of extraocular involvement. Physical examination revealed no lymphadenopathy or hepatosplenomegaly. Complete blood cell count, differential cell count, and serum chemistry test results were normal. Lumbar puncture, bone marrow biopsy, whole-body gallium scan, and computed tomography of the brain, chest, and abdomen were all unremarkable. IgM titers for EBV were positive at 1:640 and EBV DNA was present in whole blood by polymerase chain reaction amplification. Elective tonsillectomy was performed and demonstrated only reactive lymphoid hyperplasia. At 6 months of follow-up, there has been no evidence of intraocular or systemic recurrence.

**COMMENT**

Posttransplantation lymphoproliferative disorder has been shown to be associated with active EBV infection, with the highest risk if primary infection occurs after the initiation of immunosuppression. Patients often have signs and symptoms similar to those of mononucleosis (fever, malaise, pharyngitis, lymphadenopathy, hepatosplenomegaly, and neutropenia).

Only 3 cases of intraocular PTLD have been reported. Brodsky et al described decreased vision, bilateral iris tumors, and panuveitis in a 7-year-old girl who had undergone liver transplantation 3 years previously. She was receiving 200 mg of cyclosporine per day. The polyclonal tumor was resected and subsequent radiation therapy totaling 20 Gy was administered. After cataract extraction in the right eye, final visual acuities were 20/60 OD and 20/30 OS. Robinson et al described a 4-year-old girl who received cyclosporine, azathioprine, and prednisolone and developed bilateral uveitis and visual loss associated with pigmented nodules at the pupillary margin less than 1 year after liver transplantation. The patient was treated by incisional biopsy followed by a decrease in immunosuppression therapy, and she was asymptomatic at final follow-up. One additional case of PTLD...
manifesting as choroidal masses in an adult lung transplantation patient has also been reported, but its clinical characteristics were much more typical of malignant lymphoma.5

To our knowledge, this case represents the youngest patient with intraocular PTLD in the setting of solid organ transplantation. Unlike previously reported cases, our patient was receiving only minimal immunosuppressive therapy and had isolated, monocular disease that was not associated with clinically significant inflammation or visual loss.

In addition to minimizing systemic immunosuppression, resection of PTLD-associated tumors has been successful in eradicating localized disease,2 including intraocular lesions.3 Other treatment modalities include radiotherapy, systemic antiviral treatment, and immunomodulation. Despite these measures, the PTLD-associated mortality rate is approximately 50%. Thus, prevention of PTLD through minimizing immunosuppression, vaccination against EBV, and prophylactic antiviral therapy has been advocated.2

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REFERENCES


A look at the past . . .

Guyton-Reese-Retinal Diseases: Discussion

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The roentgen treatment of hemorrhagic alterations of the retina dates back to the end of the second decade of this century; curiously, it was through analogy with the good results obtained in the treatment of hemorrhages in cases of myoma uteri that Hessberg, in 1919, tried the roentgen treatment for hemorrhagic glaucoma. In the following years roentgen irradiation for hemorrhagic conditions of the fundus has met with increasing favor. However, there appears still to be considerable difference of opinion regarding the results. A substantial group, comprising the great majority of those who have reported cases of retinal hemorrhages treated with roentgen radiation, seems to approve of the method and advocates the use of small doses, totaling 600 r, or even less.